1: Peptides. 1986 Sep-Oct;7(5):849-54. Related Articles, Link

A fragment of vasoactive intestinal peptide, VIP(10-28), is an antagonist of VIP in the colon carcinoma cell line, HT29.

Turner JT, Jones SB, Bylund DB.

The 19 amino acid carboxyl terminus fragment of vasoactive intestinal peptide (VIP), VIP(10-28), inhibits [125I]VIP binding in intact HT29 colonic adenocarcinoma cells and in membranes from these cells. However, VIP(10-28) alone has no effect on adenylate cyclase activity (membranes) or cyclic AMP synthesis (intact cells) in HT29 cells although VIP receptor agonists are markedly stimulatory. The indicated antagonist character of VIP(10-28) was confirmed by rightward parallel shifts of VIP dose response curves in the presence of VIP(10-28) in adenylate cyclase and cyclic AMP synthesis experiments. The equilibrium dissociation constant values for VIP(10-28) from these experiments agree with values from inhibition binding studies. The lack of effect of VIP(10-28) on forskolin dose response curves in HT29 adenylate cyclase assays indicates the specificity of the VIP(10-28) antagonism, thus suggesting that VIP(10-28) may be a useful tool in studying VIP receptor regulation and other aspects of the mechanisms of VIP action. The potential regulatory role of a proteolytically generated fragment of VIP acting antagonistically at VIP receptors is discussed.

PMID: 3025826 [PubMed - indexed for MEDLINE]

1: Endocrinology. 1989 Dec;125(6):3109-14. Related Articles, Link

Comparison of the effects of various C-terminal and N-terminal fragment peptides of glucagon-like peptide-1 on insulin and glucagon release from the isolated perfused rat pancreas.

Suzuki S, Kawai K, Ohashi S, Mukai H, Yamashita K.

Department of Internal Medicine, Institute of Clinical Medicine, University of Tsukuba, Japan.

Truncated glucagon-like peptide-1 (GLP-1) possesses a potent stimulatory activity for insulin secretion and a slight inhibiting activity for glucagon secretion. The aim of this paper is to examine the activities of N- and C-terminal fragments of GLP-1 using a rat pancreas perfusion system. Concerning the N-terminal portion, GLP-1(7-37) amide elicited a clear insulinotropic activity at 0.1 or 1 nM with the perfusate containing 5.5 mM glucose and 5 mM arginine, while 10 nM GLP-1-(1-37) amide, -(6-37) amide, and -(8-37) amide did not. Concerning the C-terminal portion, GLP-1 (7-37) amide, -(7-37), and -(7-36) amide had a similar potency of insulinotropic activity, and GLP-1-(7-35) was less potent; 0.1 nM GLP-1-(7-35) did not stimulate insulin release, nor did 10 nM GLP-1-(7-20). Glucagon release was significantly suppressed by 1 and 10 nM GLP-1-(7-37) amide, 1(nM GLP-1-(7-37), and 1 nM GLP-1-(7-36) amide. Other fragment peptides of GLP-1, including GLP-1-(7-35), had no effect. From these results it is concluded that histidine at position 7 of GLP-1 as a free N-terminal amino acid is very important in GLP-1's insulinotropic activity and probably in glucagon-inhibiting activity, and that C-terminal amidation and three C-terminal amino acids are less important for these activities.

PMID: 2684616 [PubMed - indexed for MEDLINE]

2: Proc Natl Acad Sci U S A. 1984 Aug;81(16):5007-11. Related Articles, Link

Conversion of proglucagon in pancreatic alpha cells: the major endproducts are glucagon and a single peptide, the major

proglucagon fragment, that contains two glucagon-like sequences.

Patzelt C, Schiltz E.

It has previously been shown by biosynthetic labeling studies that glucagon i synthesized in mammalian islets via an 18-kDa precursor, proglucagon, that during processing gives rise to glucagon and a secreted peptide of 10 kDa (the major proglucagon fragment, MPGF). We have now developed a simple procedure for the isolation of this peptide from rat pancreatic islets and have characterized it more fully. On the basis of its amino acid composition, MPGF is identified as the COOH-terminal portion of proglucagon that contains two glucagon-related sequences. These sequences do not appear to be liberated from MPGF in alpha cells of the islets of Langerhans but MPGF may be processed further elsewhere in the body or in other cells of the gastrointestinal tract that produce glucagon precursors.

PMID: 6382256 [PubMed - indexed for MEDLINE]

3: Biochem Pharmacol. 1976 Jan 15;25(2):210-1. Related Articles, Link

Effect of glucagon and its 1-23 peptide fragment on lipolysis in isolated rat and human fat cells.

Mitznegg P, Domschke W, Domschke S, Sprugel W, Estler CJ, Wunsch E, Jaeger E, Demling L.

PMID: 1259784 [PubMed - indexed for MEDLINE]

4: Proc Natl Acad Sci U S A. 1973 Aug;70(8):2321-5. Related Articles, Link

Isolation of a glucagon-containing peptide: primary structure of a possible fragment of proglucagon.

Tager HS, Steiner DF.

PMID: 4525166 [PubMed - indexed for MEDLINE]

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1: Dig Dis Sci. 1989 May;34(5):703-8.

GLP-1 (glucagon-like peptide 1) and truncated GLP-1, fragments of human proglucagon, inhibit gastric acid secretion in humans.

Schjoldager BT, Mortensen PE, Christiansen J, Orskov C, Holst JJ.

Institute of Medical Physiology C, Panum Institute, Copenhagen, Denmark.

Glucagon-like peptide 1 amide (GLP-1 amide), a predicted product of the glucagon gene (proglucagon 72-107-amide), and truncated GLP-1 (proglucagon 78-107-amide), recently isolated from porcine small intestine, were infused in doses of 100 and 400 ng/kg/hr and 12.5 and 50 ng/kg/hr, respectively, into eight volunteers to study pharmacokinetics and effects on pentagastrin-stimulated gastric acid secretion (plateau stimulation with pentagastrin at D50: 100 ng/kg/hr). The concentration of GLP-1 in plasma increased from 64 +/- 12 to 189 +/- 23 and 631 +/- 76 pmol/liter, respectively The concentration of truncated GLP increased from approximately 7 pmol/liter to 28 +/- 3 pmol/liter during the high rate of infusion. A similar increase was seen in response to a mixed meal in eight normal volunteers. The metabolic clearance rate (MCR) of GLP-1 was 2.2 +/- 0.3 and 2.6 +/- 0.3 ml/kg/min, respectively, and the half-life in plasma was 17 +/- 2 min. The MCR of truncated GLP-1 was 13 +/- 2.8 ml/kg/min and the half-life 11.4 +/- 2.1 min. GLP-1 reduced the pentagastrin-stimulated acid secretion 16 +/- 9% during the low-rate infusion and 23 +/- 12% during the high rate (P less than 0.05). Truncated GLP-1 caused a 36 +/- 3% inhibition during the high infusion rate. Thus truncated GLP-1, a naturally occurring peptide, is a poten inhibitor of acid secretion in man and more so than GLP-1.

PMID: 2714145 [PubMed - indexed for MEDLINE]

1: Endocrinology. 1969 Sep;85(3):610-1. Related Articles, Link

Lipolytic activity of a peptide fragment of porcine secretin.

Rudman D, Del Rio AE.

PMID: 4183119 [PubMed - indexed for MEDLINE]

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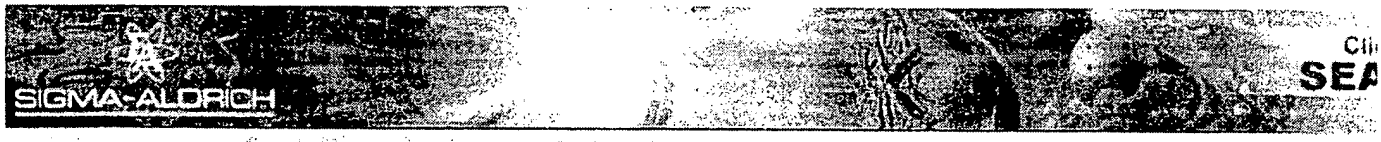

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Vasoactive Intestinal Peptides

Product Name

Helodermin >90% (HPLC), Ethanol solution

Pituitary adenylate cyclase activating polypeptide-38

Pituitary adenylate cyclase activating polypeptide amide fragment 6-27

Pituitary adenylate cyclase activating polypeptide-27 ovine minimum 97% (HPLC), Solid

Vasoactive Intestinal Peptide human, porcine, rat, minimum 95% (HPLC), Powder

Vasoactive Intestinal Peptide human, porcine, rat, minimum 95% (HPLC), Powder

Vasoactive Intestinal Peptide fragment 1-12 human, porcine, rat minimum 97% (HPLC)

Vasoactive Intestinal Peptide Fragment 6-28 human, porcine, rat minimum 97% (HPLC)

Vasoactive Intestinal Peptide Fragment 10-28 human, porcine, rat acetate salt minimum 97% (HPLC)

[Lys^{1}, $Pro^{2,5}$, $Arg^{3,4}$, Tyr^{6}]-Vasoactive Intestinal Peptide human, porcine, rat minimum 97% (HPLC)

[D-p-Cl-Phe^{6}, Leu^{17}]-Vasoactive Intestinal Peptide human, porcine, rat minimum 97% (HPLC)

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1: Biochimie. 1998 Apr;80(4):289-93. Related Articles, Link

ELSEVIER FULL-TEXT ARTICLE

An improved method to obtain a single recombinant vasoactive intestinal peptide (VIP) analog.

Ottavi A, Tiennault E, Maftah A, Berjeaud JM, Cenatiempo Y, Julien R

CNRS ESA 6031, IBMIG Universite de Poitiers, France.

The vasoactive intestinal peptide (VIP) is an ubiquitous peptide of great potential for applications. Development of new bioactive VIP analogs using production in recombinant E coli has been carried out in our laboratory. This work presents a new multimeric fusion protein expressing several VIP units separated by factor Xa cleavage site linkers. The steps leading from the affinity purification of the fusion protein and its processing by the factor Xa to the full characterization of the new bioactive improved VIP analog are also described.

PMID: 9672747 [PubMed - indexed for MEDLINE]

2: Endocrinology. 1994 May;134(5):2121-5. Related Articles, Link

Stearyl-norleucine-vasoactive intestinal peptide (VIP): a novel VIP analog for noninvasive impotence treatment.

Gozes I, Reshef A, Salah D, Rubinraut S, Fridkin M.

Department of Chemical Pathology, Sackler School of Medicine, Tel Aviv University, Israel.

The present report relates to pharmaceutical composition for the treatment of male impotence. The transdermal application of a potent derivative of vasoactive intestinal peptide (VIP) coupled to a suitable hydrophobic moiety (e.g. stearyl-VIP) in a suitable ointment composition (e.g. Sefsol) enhances sexual activity and erection formation in a variety of impotence models in rats (sterile rats, diabetic rats, and animals with high blood pressure).

Furthermore, exchange of the methionine in position 17 with norleucine enhances biological activity. Thus, stearyl-Nle17-VIP may be considered useful for the treatment of impotence.

PMID: 8156912 [PubMed - indexed for MEDLINE]

1: Metabolism. 1999 Feb;48(2):252-8.

Long-lasting antidiabetic effect of a dipeptidyl peptidase IV-resistant analog of glucagon-like peptide-1.

Burcelin R, Dolci W, Thorens B.

Institute of Pharmacology and Toxicology, Lausanne, Switzerland.

Glucagon-like peptide-1(7-37) (GLP-1) is the most potent insulinotropic hormone characterized thus far. Because its activity is preserved in non-insulin-dependent diabetes mellitus (NIDDM) patients, it is considered a potential new drug for the treatment of this disease. One limitation in its therapeutic use is a short half-life in vivo (5 minutes), due in part to a fast degradation by the endoprotease dipeptidylpeptidase IV (DPPIV). Recently, it was reported that GLP-1 became resistant to DPPIV when the alanine residue at position 8 was replaced by a glycine (GLP-1-Gly8). We report her that this change slightly decreased the affinity of the peptide for its receptor (IC50, 0.41 +/- 0.14 and 1.39 +/- 0.61 nmol/L for GLP-1 and GLP-1-Gly8, respectively) but did not change the efficiency to stimulate accumulation of intracellular cyclic adenosine monophosphate (cAMP) (EC50, 0.25 +/- 0.05 and 0.36 +/- 0.06 nmol/L for GLP-1 and GLP-1-Gly8, respectively). Second, we demonstrate for the first time that this mutant has an improved insulinotropic activity compared with the wild-type peptide when tested in vivo in an animal model of diabetes. A single injection of 0.1 nmol GLP-1-Gly8 in diabetic mice fed a high-fat diet can correct fasting hyperglycemia and glucose intolerance for several hours, whereas the activity of 1 nmol GLP-1 vanishes a few minutes after injection. These actions were correlated with increased insulin and decreased glucagon levels. Interestingly, normoglycemia was maintained over a period that was longer than the predicted peptide half-life, suggesting a yet undescribed long-term effect of GLP-1-Gly8. GLP-1-Gly8 thus has a markedly improved therapeutic potential compared with GLP-1, since it can be used at much lower doses an with a more flexible schedule of administration.

PMID: 10024091 [PubMed - indexed for MEDLINE]

2: J Endocrinol. 1998 Oct;159(1):93-102. Related Articles, Link

JOE Online

A synthetic glucagon-like peptide-1 analog with improved plasma stability.

Ritzel U, Leonhardt U, Ottleben M, Ruhmann A, Eckart K, Spiess J, Ramadori G.

Department of Medicine, Division of Gastroenterology and Endocrinology, University of Gottingen, Gottingen, Germany.

Glucagon-like peptide-1 (GLP-1) is the most potent endogenous insulin-stimulating hormone. In the present study the plasma stability and biological activity of a GLP-1 analog, [Ser]GLP-1(7-36)amide, in which the second N-terminal amino acid alanine was replaced by serine, was evaluated in vitro and in vivo. Incubation of GLP-1 with human or rat plasma resulted in degradation of native GLP-1(7-36)amide to GLP-1(9-36)amide, while [Ser] GLP-1(7-36)amide was not significantly degraded by plasma enzymes. Usin glucose-responsive HIT-T15 cells, [Ser]GLP-1(7-36)amide showed strong insulinotropic activity, which was inhibited by the specific GLP-1 receptor antagonist exendin-4(9-39)amide. Simultaneous i.v. injection of [Ser]GLP-1 (7-36)amide and glucose in rats induced a twofold higher increase in plasma insulin levels than unmodified GLP-1(7-36)amide with glucose and a fivefol higher increase than glucose alone. [Ser]GLP-1(7-36)amide induced a 1.5-fold higher increase in plasma insulin than GLP-1(7-36)amide when given 1 h before i.v. application of glucose. The insulinotropic effect of [Ser]GLP-1 (7-36)amide was suppressed by i.v. application of exendin-4(9-39)amide. Th present data demonstrate that replacement of the second N-terminal amino acid alanine by serine improves the plasma stability of GLP-1(7-36)amide. The insulinotropic action in vitro and in vivo was not impaired significantly by this modification.

PMID: 9795346 [PubMed - indexed for MEDLINE]

3: J Pharm Sci. 1997 Jul;86(7):768-73. Related Articles, Link

InterScience

A radioimmunoassay for LY315902, an analog of glucagon-like insulinotropic peptide, and its application in the study of canine pharmacokinetics.

Chou JZ, Place GD, Waters DG, Kirkwood JA, Bowsher RR.

Department of Drug Disposition, Lilly Research Laboratories, Eli Lilly & Company, Indianapolis, IN 46285, USA.

Glucagon-like insulinotropic peptide (GLP-1) and its analogs are of interest because of their therapeutic potential in type II diabetes. LY315902 is a GLP

1-(7-37)-OH analog with a modified N-terminus (IP7), an octanoic acid (C8) acylated on the lysine residue at position 34, and a substitution with arginine at position 26. We developed a sensitive and specific radioimmunoassay (RIA) for the determination of immunoreactive LY315902 in the plasma of animals. A homobifunctional cross-linker was used to couple the nonacylate form of LY315902 [IP7-R26-GLP-1-(7-37)-OH] to carrier proteins to enhance its immunogenicity. Following immunization, animal antisera were screened by RIA for the presence of LY315902 antibodies. One rabbit produced a high-affinity antiserum that display insignificant cross-reactivity against two forms of native GLP-1 and possible major metabolites of LY315902. In this RIA method, plasma samples were combined with radioiodinated LY315902 and rabbit anti-IP7-R26-GLP-1-(7-37)-OH serum, and then incubated overnight at room temperature. The bound forms of LY315902 were separated by polyethylene glycol assisted second antibody precipitation. The sensitivity of the assay was estimated to be 19 pM. Inter-assay precision (%CV) and accuracy (recovery) for quality control samples i dog plasma ranged from 8.0% to 14.7% and 92.8% to 107.3%, respectively. By applying this assay to measure plasma concentrations of immunoreactive LY315902 in dogs following twice daily subcutaneous injections of LY315902, we determined that the plasma half-life of LY315902 is significantly longer than that of native GLP-1-(7-37)-OH. We concluded that the structural modifications which were made to produce LY315902 prolonged its plasma half-life. The extended plasma half-life of LY315902 correlated well with its prolonged pharmacology in dogs.

PMID: 9232514 [PubMed - indexed for MEDLINE]

Search Result

Product	Cat#	Sequence	Weight
Prepro VIP (81-122), human	48-1-15A	His-Ala-Asp-Gly-Val-Phe-Thr-Ser-Asp-Phe-Ser-Lys-Leu-Leu-Gly-Gln-Leu-Ser-Ala-Lys-Lys-Tyr-Leu-Glu-Ser-Leu-Met-Gly-Lys-Arg-Val-Ser-Ser-Asn-Ile-Ser-Glu-Asp-Pro-Val-Pro-Val	0.5 mg
Prepro VIP (81-122), human	48-1-15B	His-Ala-Asp-Gly-Val-Phe-Thr-Ser-Asp-Phe-Ser-Lys-Leu-Leu-Gly-Gln-Leu-Ser-Ala-Lys-Lys-Tyr-Leu-Glu-Ser-Leu-Met-Gly-Lys-Arg-Val-Ser-Ser-Asn-Ile-Ser-Glu-Asp-Pro-Val-Pro-Val	1.0 mg
Prepro VIP /PHM (111-122)	48-1-30A	Val-Ser-Ser-Asn-Ile-Ser-Glu-Asp-Pro-Val-Pro-Val	1.0 mg
Prepro VIP /PHM (111-122)	48-1-30B	Val-Ser-Ser-Asn-Ile-Ser-Glu-Asp-Pro-Val-Pro-Val	5.0 mg
Prepro VIP /PHM (156-170)	48-1-31A	Ser-Ser-Glu-Gly-Glu-Ser-Pro-Asp-Phe-Pro-Glu-Glu-Leu-Glu-Lys	1.0 mg
VIP (11-28), human, porcine, rat, ovine	48-1-25A	Thr-Arg-Leu-Arg-Lys-Gln-Met-Ala-Val-Lys-Lys-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	0.5 mg
VIP (11-28), human, porcine, rat, ovine	48-1-25B	Thr-Arg-Leu-Arg-Lys-Gln-Met-Ala-Val-Lys-Lys-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	1.0 mg
VIP Receptor Binding Inhibitor	48-1-35A	Leu-Met-Tyr-Pro-Thr-Tyr-Leu-Lys	1.0 mg
VIP, guinea pig	48-6-15A	His-Ser-Asp-Ala-Leu-Phe-Thr-Asp-Thr-Tyr-Thr-Arg-Leu-Arg-Lys-Gln-Met-Ala-Met-Lys-Lys-Tyr-Leu-Asn-Ser-Val-Leu-Asn-NH2	0.5 mg
VIP, guinea pig	48-6-15B	His-Ser-Asp-Ala-Leu-Phe-Thr-Asp-Thr-Tyr-Thr-Arg-Leu-Arg-Lys-Gln-Met-Ala-Met-Lys-Lys-Tyr-Leu-Asn-Ser-Val-Leu-Asn-NH2	1.0 mg
VIP, human, porcine, rat, ovine	48-1-10A	His-Ser-Asp-Ala-Val-Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Lys-Gln-Met-Ala-Val-Lys-Lys-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	0.5 mg
VIP, human, porcine, rat, ovine	48-1-10B	His-Ser-Asp-Ala-Val-Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Lys-Gln-Met-Ala-Val-Lys-Lys-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	1.0 mg
		His-Ser-Asp-Ala-Val-D-(pCl)Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Lys-Gln-Leu-Ala-	

[(4Cl)DPhe6,Leu17] VIP	48-1-28A	Val-Lys-Lys-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	1.0 mg
[Arg15,20,21, Leu17] VIP, human, porcine, rat, ovine	48-1-70A	His-Ser-Asp-Ala-Val-Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Arg-Gln-Leu-Ala-Val-Arg-Arg-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	0.5 mg
[Arg15,20,21, Leu17] VIP, human, porcine, rat, ovine	48-1-70B	His-Ser-Asp-Ala-Val-Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Arg-Gln-Leu-Ala-Val-Arg-Arg-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	1.0 mg
[Arg15,20,21, Leu17] VIP-Gly-Lys-Arg-NH2	48-1-75A	His-Ser-Asp-Ala-Val-Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Arg-Gln-Leu-Ala-Val-Arg-Arg-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-Gly-Lys-Arg-NH2	0.5 mg
[Arg15,20,21, Leu17] VIP-Gly-Lys-Arg-NH2	48-1-75B	His-Ser-Asp-Ala-Val-Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Arg-Gln-Leu-Ala-Val-Arg-Arg-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-Gly-Lys-Arg-NH2	1.0 mg
[Lys1, Pro2,5,Arg3,4,Tyr6] VIP, human, porcine, rat, ovine	48-6-31A	Lys-Pro-Arg-Arg-Pro-Tyr-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Lys-Gln-Met-Ala-Val-Lys-Lys-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	0.5 mg
[Lys1, Pro2,5,Arg3,4,Tyr6] VIP, human, porcine, rat, ovine	48-6-31B	Lys-Pro-Arg-Arg-Pro-Tyr-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Lys-Gln-Met-Ala-Val-Lys-Lys-Tyr-Leu-Asn-Ser-Ile-Leu-Asn-NH2	1.0 mg

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